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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,452	10/31/2000	David B. Weiner	UPAP0011-100	6483

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/622,452	WEINER ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6,7,9-12,15,17,18,33,36,42,43,46,49,50 and 52-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,12,17,33,46,49,53,54 and 56* is/are rejected.

7)☒ Claim(s) *4,7,9-11,15,18,33,36,42,43,46,49,50,52 and 55-58* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response received on 12/17/09 has been entered. Claims 2-3, 5, 8, 13-14, 16, 19-32, 34-35, 37-41, 44-45, 47-48, and 51 are canceled. Claims 1, 4, 6-7, 9-12, 15, 17-18, 33, 36, 42-43, 46, 49-50, and 52-58 are currently pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Claim Rejections - 35 USC 102

The rejection of claims 1, 6, 12, 17, and 53-54 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,417,328 (7/9/02), hereafter referred to as Alnemri, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection of record for reasons of record as discussed in detail below..

The applicant reiterates their previous argument that Alnemri et al. does not teach a "pyrogen free" composition, and that while Alnemri teaches "expressible nucleic acids encoding DR5", the current claims recite a plasmid comprising a nucleic acid encoding DR5 and an immunogen. The applicant also states that Alnemri et al. provides no suggestion to use a plasmid encoding DR5 and a pathogen antigen *in vivo*. The applicant further reiterates their previous argument that a reading of the section in Alnemri about physiological carriers, i.e. columns 22-

23, has nothing to do with the disclosure elsewhere in the document of reagents for experimentation, such that Alnemri et al. fails to teach the invention as arranged in the claim, citing *Net MoneyIN, Inc. v. VeriSign, Inc.,* and *In re Arkley*.

In response, Alnemri et al. clearly teaches a plasmid encoding DR5 and the immunogen LacZ, which is a bacterial antigen, i.e. an immunogen which is a pathogen antigen, or the combination of the plasmid encoding DR5 and the plasmid encoding CrmA, a viral protein antigen which is also an immunogen derived from a pathogen, and further provides teachings for making a sterile aqueous solution in columns 22-23. Note that as there is no requirement that the a prior art reference must set forth the claimed invention *in haec verba,* it is irrelevant that Alnemri et al. does not use the phrase "pyrogen free" as Alnemri et al. clearly teaches sterile aqueous solutions of the disclosed plasmids which meet the definition of "pyrogen free", as discussed in detail in previous office actions. In particular, the previous office action discussed that fact that Alnemri broadly teaches to prepare "expressible nucleic acids encoding DR5" as sterile aqueous solutions that do not contain any material other than the nucleic acid and water or physiological saline (column 23, lines 12-17). Since Alnemri et al. teaches that the solution does not contain anything other than nucleic acid and water or physiological saline, the solution cannot by Alnemri's own definition contain a pyrogen. Thus, the solutions taught by Alnemri et al. qualify as "pyrogen-free".

In regards to improperly combining teachings from two unrelated sections of the Alnemri disclosure, it is reiterated that the disclosure in column 22 concerning therapeutic compositions of DR5 refers specifically to "expressible nucleic acids encoding DR5". As stated in previous office actions, the plasmids exemplified in columns 27-28 are in fact expressible nucleic acids.

Further, as noted above Alnemri broadly teaches to prepare "expressible nucleic acids encoding DR5" as sterile aqueous solutions that do not contain any material other than the nucleic acid and water or physiological saline (column 23, lines 12-17). As such, the teachings in columns 22-23 to prepare sterile aqueous solutions of the nucleic acids read on the particular plasmids disclosed in the examples. Further, the applicant is reminded that the instant claims under rejection, claims 1, 6, 12, 17, and 53-54, are all product claims and are not limited to any particular intended use. Although applicant argues that the plasmids in the examples are used in *in vitro* experiments, and not *in vivo* such that the skilled artisan would not look to these plasmids when making pharmaceutical compositions, this is not persuasive since as noted above and in previous office actions Alnemri et al. teaches to make pharmaceutical compositions of any expressible nucleic acid encoding DR5 noted limited to any particular plasmid or expression vector and thus includes the plasmids set forth in the examples section of Alnemri et al. Thus, applicant's arguments that Alnemri et al. does not specifically teach to use the exact plasmids set forth in the working examples in *in vivo* assays or for diagnosing or treating disease is not found persuasive.

Therefore, for reasons of record as discussed in detail above, the rejection stands.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 6, 12, 17 and 53-54 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,417,328 (7/9/02), hereafter referred to as Alnemri, in view of U.S. Patent No. 5,693,622 (12/2/97), hereafter referred to as Wolff et al. is maintained.

Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection of record for reasons of record as discussed in detail below.

The applicant reiterates their previous arguments that there is no motivation to make a pyrogen free plasmid encoding DR5 in either Alnemri or Wolff. In response, Alnemri specification broadly teaches to prepare "expressible nucleic acids encoding DR5" as sterile aqueous solutions that do not contain any material other than the nucleic acid, water or physiological saline. Thus the teachings in column 22 to prepare sterile aqueous solutions of the nucleic acids reads on the particular plasmids disclosed in the examples, which include a single plasmid encoding DR5 and the bacterial pathogen immunogen LacZ or the combination of a plasmid encoding DR5 and a plasmid encoding CrmA, a viral pathogen antigen, regardless of whether they were actually used in *in vitro* experiments versus *in vivo* methods. The fact that Wolff et al. does not disclose the use of DR5 is irrelevant as Alnemri et al. provides this teaching and Wolff et al. is cited to provide teachings for the standard methods of preparing plasmid DNA for pharmaceutical use. Therefore, it is maintained that in view of the teachings of Alnemri et al. to prepare a sterile pharmaceutical composition comprising a plasmid(s) encoding DR5 for administration to a mammal, and the teachings of Wolff et al. for standard methods for plasmid DNA preparation for *in vivo* use, it would have been *prima facie* obvious to the skilled artisan at the time of filing to use the well known and widely practiced methods taught by Wolff et al. to prepare the plasmids encoding DR5 and an immunogen taught by Alnemri et al.. Further, based on the standard nature of cesium chloride purification, and the high level of skill in the art of molecular biology at the time of filing, the skilled artisan would have had a reasonable expectation of success in producing a pyrogen-free composition containing the plasmid(s) taught

by Alnemri et al. using the purification method taught by Wolff et al. Therefore, the rejection of record is maintained.

Claim Rejections - 35 USC 112

The rejection of claim 11 under 35 U.S.C. 112, first paragraph, for scope of enablement, is withdrawn in view of applicant's amendments to claim 11.

The rejection of claims 33, 36, 52, and 55-58 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn in view of the amendment to claims 33 and 56.

Claim Objections

Claims 4, 7, 9-11, 15, 18, and 42-43 are objected to as being dependent upon a rejected base claim, but would be allowable based on the elected species of DR5 as the immunomodulating protein if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Further, as set forth in previous actions in the interests of compact prosecution, it is again noted that should applicant limit claims 4, 7, 9-11, 15, 18, 33, 36, 42-43, 46, 49-50, 52, and 55-58 to the elected subject matter of DR5, and rewrite all claims dependent on rejected claims 1, 6, and 12 in independent form as noted in the preceding paragraph, the

subject matter of claims 4, 7, 9-11, 15, 18, 33, 36, 42-43, 46, 49-50, 52, and 55-58 would be considered free of the prior art of record and allowable.

The objection to pending claims 1, 4, 6-7, 9-12, 15, 17-18, 33, 36, 42-43, 46, 49-50, and 52-58 for continuing to recite non-elected subject matter, there being no allowable generic claim, is maintained. The applicant argues that all the claims recite the elected species and that once this species is found to be allowable that the generic claims and a reasonable number of non-elected species be examined and allowed. In response, it is first noted that all the instant claims have not been found allowable based on examination of the elected species of DR5. Further, MPEP 809.02(a) states:

> Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

As the generic claims have not been found allowable, see below, the objection to the claims remains.

In the previous office action, the applicant was advised that should claim 7 be found allowable, claim 33 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The applicant argues that claim 7 does not limit the immunogen to a pathogen. This

is incorrect. Claim 7 recites the administration of the composition of claim 1 and claim 1 clearly limits the immunogen to a pathogen antigen- see the last line of claim 1. Thus, it is maintained that claims 7 and 33 are substantial duplicates.

In the interests of compact prosecution and in an attempt to further prosecution the examiner made several rejections of record over the generic claims in the previous office action to demonstrate that the generic claims are not allowable. However, the previous office action clearly stated that the election of species requirement has NOT been withdrawn, and full examination of the claims remains based on the elected species of DR5 as the immunomodulatory molecule. The examiner provided a 102(b) rejection and a 103(a) rejection to show that the first 5 listed species in the large list of immunomodulating proteins listed in the independent generic claims were anticipated or obvious in view of the prior art. Applicant's response to this attempt to further prosecution was to cancel the first 5 species listed in the generic claims and to argue that now the generic claims are allowable. This is not agreed. Neither the elected species, nor the generic claims are allowable. See below.

In view of applicant's amendments to the generic claims to delete the first five species of immunomodulatory protein listed, the rejections under 35 U.S.C 102(b) over WO 96/36366 (1996), (Dow et al.), and under 103(a) over WO 96/36366 (1996), (Dow et al.), US Patent 6,204,250 (2001) (Bot et al.), and US Patent No. 5,494,807 (1996), (Paoletti et al.), are withdrawn.

Applicant's amendment has necessitated the following new grounds of rejection of the generic claims. The generic independent claims are 1, 6, 33, 46, 49, and 56.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6, 33, 46, 49, and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,916,879 (1999), hereafter referred to as Webster, in view of US Patent No. 5,990,301 (1999), hereafter referred to as Colpan et al.

Webster teaches one or two plasmids encoding influenza HA and an immunoeffector, and further wherein the immunoeffector is ICAM (Webster, columns 6, 11-12, and 18). Webster further teaches the plasmid or plasmids wherein one or both genes are operatively linked to a CMV promoter (Webster, columns 4, 11-12). In addition, Webster teaches methods of generating

protective immunity against influenza virus in a subject by intramuscular administration of the plasmid(s) encoding HA and an immunoeffector such as ICAM-1(Webster, columns 4-6, and 16-18).

While Webster teaches to purify the plasmid DNA for administration using Qiagen columns (Webster, columns 20-21), Webster does not specifically teach the level of purity of the plasmid DNA obtained. Colpan et al. supplements Webster by teaching particular Qiagen columns and methods which provide toxin-free, including endotoxin free, preparations of plasmid DNA suitable for therapeutic administration of genetic vaccines (Colpan et al., columns 3-5, and 9-10). Colpan et al. further teaches that their disclosed and claimed methodology is preferable to other methods of purification since the plasmid DNA obtained is free of allergic, toxic, and possibly carcinogenic substances including phenol, chloroform, ethidium bromide, and endotoxins (Colpan et al., columns 3-4).

Thus, in view of the teachings of Webster to purify plasmid DNA using a Qiagen column, and the detailed teachings of Colpan et al. for an improved method of Qiagen plasmid DNA preparation which produces endotoxin free plasmid preps for genetic vaccination, it would have been *prima facie* obvious to the skilled artisan to prepare the plasmid or plasmids taught by Webster which encode HA and ICAM-1 using the method disclosed by Colpan et al. in order to produce a purified plasmid preparation suitable for vaccination of a subject with a reasonable expectation of success, and further to administer the plasmid(s) according to the methods of Webster to induce protective immunity against Influenza.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the

USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633